

Carcinogenic Potency Database (CPDB) Plot of Aristolochic Acid

Chemical				CAS number			
Spe	Strain	Xpo+Xpt					Literature Reference
Sex	Route	RefNum			0Dose	1Dose	
Site	Notes	DR	AuOp	UpConf			
Path	TD ₅₀	2Tailpvl	LoConf		Cntrl	1Inc	
ARISTOLOCHIC ACID, SODIUM SALT (77% AA I, 21% AA II) mixture							
Mengs;artx,51,107-119;1982/pers.comm.							
1	R f wis gav	52w69	2424		0	75.0ug	
	for mix Ae	14.1ug	P<.008	+	3.89ug	.254mg	0/4 4/5
	for sqp Ae	24.7ug	P<.04		6.88ug	n.s.s.	0/4 3/5
	for sqc Ae	.101mg	P<.3	+	16.3ug	n.s.s.	0/4 1/5
2	R m wis gav	52w69	2424		0	75.0ug	
	for sqc Ae	noTD50	P<.02	+	n.s.s.	n.s.s.	0/5 4/4

Abbreviations: R = rat; f = female; m = male; wis = Wistar; gav = gavage; w = weeks; for = forestomach; sqp = squamous cell papilloma; sqc = squamous cell carcinoma

Appendix 6: Notecodes and Definitions

Code	Definition
A	Serial sacrifice experiments of Aristolochic Acid in the same paper were evaluated as positive at additional sites by the author but did not meet inclusion rules of the CPDB. See table below.

Notecode A: Aristolochic Acid

For the test of Aristolochic Acid (AA) in Wistar rats (Mengs, 1982), the CPDB includes only results of the chronic, 69 week experiment in which AA was administered at 0.1 mg/kg/day for 52 weeks. Other groups of rats were administered 1.0 or 10 mg/kg/day for only 13 weeks and were sacrificed at various times shown in the table below; this short dosing period and the short times to sacrifice do not meet the inclusion rules of the CPDB (at least 6 months dosing and 12 months experiment length). In the 69-week experiment that meets the inclusion rules, the only target site was forestomach. Kidney and bladder were additional target sites in the excluded groups that were administered higher doses for 13 weeks; tumor incidence data are given in the table below for each sacrifice time. The table reports the dose as administered for 13 weeks and not the CPDB daily dose-rate or a TD₅₀ value, because the serial sacrifice experiments do not meet the CPDB inclusion rules.

Sex	Tissue	Tumor	Exposure duration in weeks	Sacrifice time in weeks	Administered dose by gavage (mg/kg/day)			
					0	0.1	1	10
					Incidences			
f	Forestomach	sqp	13	13	0/9	0/9	8/9	10/10
		sqp,sqc	13	26	0/10	0/5	7/10	13/13
		sqp,sqc	13	39 (52)	(0/7)	(2/6)	9/11	4/4
		sqp,sqc	52 ^a	69 ^a	0/4	4/5		
	Kidney cortex	coc	13	26	0/10	0/5	0/10	2/13
		coa	13	39 (52)	(0/7)	(0/6)	0/11	4/4
	Urinary bladder	tpp,tcc	13	26	0/10	0/5	0/10	2/13
tpp		13	39 (52)	(0/7)	(0/6)	0/11	1/4	
m	Forestomach	sqp	13	13	0/9	0/9	7/9	10/10
		sqp,sqc	13	26	0/10	0/5	9/11	18/18
		sqp,sqc	13	39 (52)	(0/6)	(4/7)	9/9	
		sqc	52 ^a	69 ^a	0/5	4/4		
	Kidney/pelvis	tcc	13	26	0/10	0/5	0/11	8/18
	Kidney cortex	coa	13	39 (52)	(0/6)	(0/7)	1/9	
	Urinary bladder	tpp,tcc	13	26	0/10	0/5	0/11	6/18

^a Included in CPDB, since exposure and experiment length meet inclusion rules.

Tumor codes:coa = cortical adenoma; coc = cortical carcinoma; sqc = squamous-cell carcinoma; sqp = squamous cell papilloma; tcc = transitional-cell carcinoma; tpp = transitional-cell papilloma.

Reference

Mengs, U., Lang, W., and Poch, J.-A. The carcinogenic action of aristolochic acid in rats. *Arch. Toxicol.* 51: 107-119(1982).